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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/718,355	ROULEAU ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :4/27/07; 5/2/07; 6/22/07; 8/16/07.

DETAILED ACTION

1. The remarks and amendments filed 16 August 2007 have been entered. Claims 58 – 59 are new; claims 42 – 59 are pending and under examination.

Withdrawn Rejections and Objections

2. The following rejections and objections set forth in the previous office action are withdrawn:

A. The objection to claim 45 is withdrawn in light of the amendments thereto.

B. The rejections of claims 45, 50 – 52, and 57 under 35 USC 112, second paragraph are withdrawn in light of the amendments which clarify the scope of the claims.

C. The rejection under 35 USC 102(b) over Tian et al. is withdrawn in light of the amendments to claim 42. Claim 42 now requires that the SCN1A protein have the sequence of SEQ ID NO:3 or 4, or be encoded by the nucleic acid of SEQ ID NO:1 or 2 (which encode SEQ ID NO:3 and 4 respectively; see p. 27 of the specification). These are human sodium channel sequences. The reference by Tian teaches contacting rat tissue slices with test compounds. As the specification (p. 7) discloses that the rat sequence is 95% identical to the human sequence, the prior art reference by Tian is outside the scope of claim 42.

D. The rejection under 35 USC 102(b) over Noda is withdrawn in light of the amendments to claim 42. Claim 42 now requires that the SCN1A protein have the sequence of SEQ ID NO:3 or 4, or be encoded by the nucleic acid of SEQ ID NO:1 or 2 (which encode SEQ ID NO:3 and 4 respectively; see p. 27 of the specification). These are human sodium channel sequences. As set forth in the previous office action, the protein from Noda is 98.5% identical to SEQ ID NO:4, and therefore is outside of the scope of claim 42.

Maintained Rejections and Objections

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 42 – 47, 49 – 51, 53 – 54 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Rechkziegel (1998. Journal of Physiology 509(Pt. 1):139-150, published May 1998).

This rejection stands for the reasons of record and explained in further detail below. Briefly, Rechkziegel teaches assays comprising contacting human brain tissue, which comprises human sodium channel 1-alpha (i.e., the protein of SEQ ID NO:3) with test compounds including tetrodotoxin (TTX) and saxiotoxin (STX), assaying the activity of the sodium channel in both the presence and absence of these toxins, and selecting the toxins as inhibitors of channel activity. The reference teaches all the required starting materials and method steps recited in independent claim 42.

Applicant argues that the reference by Rechkziegel does not anticipate independent claim 42. Specifically, applicant makes the following point on pp. 9 – 11 of the remarks filed 16 August 2007:

A) Rechkziegel does not teach a selection step as required by claim 42, part (d)

B) The reference is silent as to the sequences of the sodium channel proteins and therefore cannot be anticipatory.

C) The relevant sodium channel might not be in the tissue samples described in Rechkziegel, and "[i]t appears much more conceivable that the tissue preparation of Rechkziegel comprises different mixtures of channels and not only sodium channels." (remarks, p. 10, emphasis in original)

D) The reference by Rechkziegel does not satisfy the preamble requirement of claim 42, and does not teach a sufficient correlation between the SCN1A channels and the observed changes in sodium channel activity

E) Inherency must be certain and that "reasonable" teachings are not sufficient to reject a claim based on inherency.

Applicant's arguments have been fully considered but they are not persuasive. Each of the points enumerated above will be answered below.

A) Rechkziegel in fact does teach selection as required by the claim. The step "selecting a compound which reduces activity" is broad and does not require any specific mechanical steps, such as moving a test tube from one rack to another, or marking the results on a paper. As Rechkziegel teaches that both STX and TTX inhibit sodium channel activity, the

reference teaches selection of these two toxins. This step does not require anything more than identification of the "test compound" as an inhibitor.

B) Although the reference is silent with respect to the sequence of sodium channels contained in the tissue samples, the specification itself provides evidence that the protein of SEQ ID NO:3 is present. The specification states (p. 27 lines 13 – 17) that SEQ ID NO:3 is the adult SCN1A protein; the sequence listing clearly identifies SEQ ID NO:3 as the human protein (see also specification, paragraph spanning pp. 5 – 6). The reference by Rechkziegel indicates that tissue samples were obtained from adult humans (see p. 140 first paragraph of the Methods section). The tissue is from adult humans and comprises sodium channels. Applicant is reminded that rejections based on inherency are appropriate when a prior art reference teaches the same product but is silent with respect to a property that appears to be inherent (MPEP § 2112(II) - §2112(IV)). Of course, the same logic applies to methods which require such products as starting materials (MPEP § 2112(III)). Here, the prior art teaches methods of contacting compositions comprising human adult sodium channels with test compounds as recited in claim 42 but the reference is silent as to the sequence. The specification provides evidence that human adult sodium channel 1-alpha has the sequence of SEQ ID NO:3, According to the guidance provided in MPEP § 2112(IV), rejections for inherency are appropriate when the examiner provides evidence and scientific rationale tending to show inherency:

> "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)(emphasis in original)

Thus even though the Rechkziegel reference is silent as to the sequence, the rejection is appropriate as the examiner has provided the basis required.

C) The examiner concedes it is quite likely that the tissue samples described in the Rechkziegel contain a plethora of other channels. However, that does not change the fact that the reference anticipates the method of claim 42. Claim 42 uses open language ("A method ... comprising" certain steps; "contacting a composition comprising a SCN1A channel") which allows for inclusion of other non-recited elements in the claim. While the reference by Rechkziegel certainly contains other elements, the reference still anticipates the claimed

methods. The specification discloses that the alpha subunit is the main component of the sodium channel (p. 3). The examiner has already set forth reasons why the tissue samples from Rechkziegel contain the appropriate protein.

D) Applicant argues that the teachings of Rechkziegel do not satisfy the preamble requirement of claim 42. The preamble need not necessarily be given patentable weight, particularly in those instances where it recites an intended use; see MPEP § 2111.02(II). Here, the preamble of claim 42 recites an intended use of the assay, but the specific starting materials and steps are limited by the body of the claim and not the preamble. Applicant also argues (p. 11) that the skilled artisan could not reasonably conclude that the changes in sodium channel activity are due to changes in the activity of SCN1A in particular. However the use of open claim language allows for the activities of multiple sodium channels to be compared. As STX and TTX used by Rechkziegel decrease the activities of all sodium channels, and the reference teaches measurement of channel activity in the presence and absence of these test compounds, the claim is anticipated.

E) The examiner notes that inherent features such as sequences need not be recognized at the time of the invention (MPEP § 2112(II)), and that rejections under inherency are appropriate when the reference is silent as to a characteristic or feature that appears to be inherent (MPEP § 2112(III)). In those cases, the examiner must provide "rationale or evidence tending to show inherency" (MPEP § 2112(IV)). Here, the examiner has provided the appropriate rationale, namely that the specification itself discloses that adult human SCN1A has the sequence of SEQ ID NO:3.

For the reasons above, the rejection stands with respect to claim 42. The reasons why the limitations of claims 43 – 47, 49 – 51, and 53 – 54 are taught by the reference are set forth on p. 5 of the office action mailed 16 April 2007 and for the sake of brevity will not be reiterated here. It is noted that applicant did not traverse the examiner's rejection of the dependent claims, but presented arguments as to why the independent claim is not anticipated by Rechkziegel. New claim 59, which depends from claim 42, recites a product-by-process limitation for the starting material (i.e., the protein of SEQ ID NO:3). While the reference does not teach recombinantly-produced SCN1A protein, this product is structurally identical to the endogenously-produced product which is present in the composition from Rechkziegel. The additional "recombinant" limitation in claim 59 fails to distinguish the product required for the claimed method from those used in the prior art. While claim 59 is not a product-by-process

claim per se, the starting material is defined in this manner. Such products are limited only by the structure implied by the steps used in making the product, not by the steps themselves; see MPEP § 2113.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 42 – 51, 53 – 54, and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rechkziegel (1998. Journal of Physiology 509(Pt. 1):139-150, published May 1998) in view of Hartshorne (1984. Journal of Biological Chemistry 259:1667 – 1675).

This rejection stands for the reasons previously made of record (with respect to claims 42 – 51 and 53 – 54), and is extended to new claim 59 as well. The reasons why claims 42 – 47, 49 – 51, 53 – 54, and 59 are anticipated by Rechkziegel are set forth above. The reference teaches screening sodium channels for antagonists which bind to the channels including STX and TTX, but does not teach cell-free assays as recited in claim 48.

Hartshorne teaches purifying sodium channels to homogeneity from tissue and teaches that the purified channels are able to bind STX. The reference teaches that the isolation process increases the concentration of sodium channels over 1300-fold. However Hartshorne does not explicitly teach screening methods as recited in claim 42.

It would have been obvious to one of ordinary skill in the art to use the cell-free binding assays described by Hartshorne in the screening assays of Rechkziegel, with a reasonable expectation of success. The artisan of ordinary skill would be motivated to use the purified channels and cell-free binding assay, because doing so would allow the artisan to use considerably less of the agents to be screened, thereby reducing costs. Applicant did not traverse the examiner's determination that the invention of claim 48 would have been obvious to one of ordinary skill in the art, given the teachings of Hartshorne, but rather argued that the reference by Rechkziegel does not anticipate claim 42 and that the deficiency is not corrected by Hartshorne. As set forth in the rejection under 35 USC 102(b) above, Rechkziegel teaches

every element of claim 42. The rejection of claim 48 as obvious over Rechkziegel in view of Hartshorne stands for the reasons of record.

5. Claims 42 – 47, 49 – 54, and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rechkziegel (1998. Journal of Physiology 509(Pt. 1):139-150, published May 1998) in view of Kienle (1997. Biosensors and Bioelectronics 12:779-786).

This rejection stands for the reasons previously made of record (with respect to claims 42 – 47 and 49 – 54), and is extended to new claim 59 as well. The reasons why claims 42 – 47, 49 – 51, 53 – 54, and 59 are anticipated by Rechkziegel are set forth above. The reference teaches screening sodium channels for antagonists including STX and TTX, but does not teach using surface plasmon resonance, as recited in claim 52, to detect the interaction between the putative antagonists and the channel.

Kienle teaches use of surface plasmon resonance, as recited in claim 52, to identify agents which bind to rat cardiac sodium channels, which are functionally similar to the sodium channels in claim 42. As set forth in the previous office action, the surface plasmon resonance technique allows for measurement of kinetic rate constants and affinity constants, both of which are useful for the artisan to know when developing drugs. However, Kienle does not teach screening assays using the specific sodium channels recited in claim 42.

It would have been obvious to one of ordinary skill in the art to modify the assays of Rechkziegel, which screen for antagonists that bind to sodium channels, to include the surface plasmon resonance technique taught by Kienle, with a reasonable expectation of success. Applicant did not traverse the examiner's determination that the invention of claim 52 (i.e. using surface plasmon resonance) would have been obvious to one of ordinary skill in the art, given the teachings of Kienle, but rather argued that the reference by Rechkziegel does not anticipate claim 42 and that the deficiency is not corrected by Kienle. As set forth in the rejection under 35 USC 102(b) above, Rechkziegel teaches every element of claim 42. The rejection of claim 48 as obvious over Rechkziegel in view of Kienle stands for the reasons of record.

6. Claims 42 – 47, 49 – 51, 53 – 55, and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rechkziegel (1998. Journal of Physiology 509(Pt. 1):139-150, published May 1998) in view of Avanzini (1996. Progressive Nature of Epileptogenesis (Epilepsy Res. Suppl. 12), pp. 53 – 61).

This rejection stands for the reasons previously made of record (with respect to claims 42 – 47, 49 – 51, and 53 – 55), and is extended to new claim 59 as well. The reasons why claims 42 – 47, 49 – 51, 53 – 54, and 54 are anticipated Rechkziegel are set forth above. Briefly, the reference teaches contacting brain tissue from adult humans, which comprises the protein of SEQ ID NO:3, with candidate agents and determining whether the agents reduce sodium channel activity as recited in claim 42. Rechkziegel teaches compositions which comprise SEQ ID NO:3, as recited in claims 42 and 54, but does not teach compositions comprising the juvenile form of the sodium channel, i.e. that "obtained from a nucleic acid encoding SEQ ID NO:4" as recited in claim 55.

As set forth in the previous office action, Avanzini teaches contacting tissue comprising juvenile rat sodium channels with TTX (p. 54 second column). However Avanzini does not teach performing screening assays to find drugs which reduce sodium channel activity in tissue from juvenile humans.

It would have been obvious to one of ordinary skill in the art to modify the experiments of Rechkziegel to use neonatal human tissue rather than adult human tissue, as suggested by Avanzini, thereby arriving at the screening assay wherein a composition comprising SEQ ID NO:4, the neonatal form of the SCN1A channel, is present and therefore on point to claim 55. Applicant did not traverse the examiner's determination that the invention of claim 55 (i.e. using tissue samples comprising juvenile human sodium channels) would have been obvious to one of ordinary skill in the art, given the teachings of Avanzini, but rather argued that the reference by Rechkziegel does not anticipate claim 42 and that the deficiency is not corrected by Avanzini. As set forth in the rejection under 35 USC 102(b) above, Rechkziegel teaches every element of claim 42. The rejection of claim 48 as obvious over Rechkziegel in view of Avanzini stands for the reasons of record.

Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56 – 58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of claims 56 – 58 depends directly or ultimately from claim 42, which requires 100% identity to SEQ ID NO:3 or 4 or to the amino acids encoded by SEQ ID NO:1 or 2. However, claims 56 – 58 each expand, rather than narrow, the scope of claim 42 as they allow for variants in the sodium channel sequence. The skilled artisan could not determine the scope of claims 56 – 58 because on the one hand they depend from claim 42 and should incorporate all the limitations of the parent claim, but claims 56 – 58 are also broader than claim 42 because they encompass methods of using proteins less than 100% identical to the sequences recited in claim 42.

Conclusion

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Daniel E. Kolker, Ph.D.
October 11, 2007

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER